Development of the Gap Measure of Tinnitus: Animal and Human Studies

Jeremy Turner[1,2], Bret Eschman[1], Kyle Alberssen[1], John Manker[1]

[1]Illinois College [2]Southern Illinois University School of Medicine Dept of Surgery/Otolaryngology

SIU School of Medicine
Otolaryngology - Head & Neck Surgery

Auditory Research Group
Southern Illinois University School of Medicine

US Department of Defense International State-of-the-Science Meeting on Blast-Related Tinnitus (Nov. 2011)

Background

Noise and chemical exposure consistent with tinnitus results in deficits in laboratory animal's ability to detect silent gaps embedded in a background noise (Turner et al., 2006, Turner, 2007, Turner & Parrish, 2008; Yang et al., 2007). This technique has generally been referred to as the "gap" method for short, or the gap prepulse inhibition of acoustic startle (GPIAS) method. The deficits in processing the silence are consistent with the presence of tinnitus, and because the frequency content of the background carrier can be changed it is possible to assemble a putative tinnitus frequency range where silent deficits are present. Altering the background intensity can be also be done, possibly serving to estimate the relative intensity of the tinnitus percept. These deficits appear to be the results of tinnitus and not hearing loss when control hearing testing shows that the animal processes the background carrier stimulus normally using prepulse inhibition. ABR thresholds can also be used to determine the presence and location of gross hearing deficits relative to tinnitus deficits. Some benefits of the method include that the data can be collected very rapidly. Our laboratory can do a full scan for tinnitus across 10 different frequencies in up to 8 animals in less than one hour. Because the method makes use of a reflex, there is no learned response to train or maintain, it requires no food or water restriction or aversive shock, and allows many animals to be tested simultaneously in a short session. The measure can also be repeatedly collected across the lifespan, lending itself well to longitudinal aging studies. Because the startle reflex is so well conserved across species, the method also lends itself well to comparative studies of tinnitus across species. The current poster highlights some of these key features of the method and presents some comparative data in lab animals and early data from humans.

SIU Med Laboratory funded by a grant from the Tinnitus Research Consortium. Behavioral equipment (patent pending) donated by Kinder Scientific in the memory of SIU graduate Dorothy Jean Kinder (Walker).

Methods

Figure 1. Normal hearing animals exhibit an inhibited startle reflex when a silent gap is embedded in background.

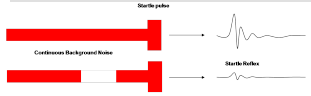
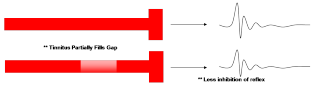


Figure 2. Following noise or chemical exposure to induce tinnitus, animals exhibit less inhibition of startle when the background matches their putative tinnitus, presumably because their tinnitus partially degrades the "signal-to-noise" for detection of the silent gap cue.



Salicylate-Induced Tinnitus in Lab Animals

Figure 3. Mice show tinnitus-like deficits in processing a silent gap following a 300 mg/kg i.p. injection of salicylate. Silent gap embedded in a broadband noise, 45 dB carrier.

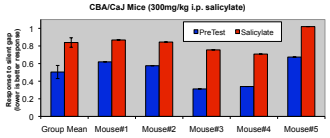


Figure 4. Guinea pigs show tinnitus-like deficits processing a silent gap following a 300 mg/kg i.p. injection of salicylate. Silent gap embedded in a 4,000 Hz, 60 dB carrier.

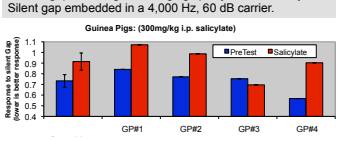
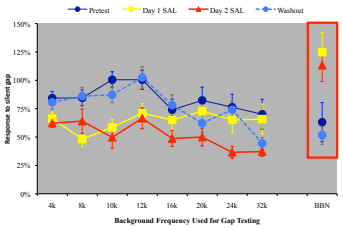


Figure 5. Rats (n=10) showed tinnitus-like deficits (circled) in processing a silent gap after one and two days of receiving a 350 mg/kg i.p. injection. Silent gap embedded in a broadband noise, 60 dB carrier. Notice the gap deficits for BBN (putative tinnitus) but the simultaneous improvements with the frequency-specific carriers (putative hyperacusis). Adapted from Turner & Parrish, 2007.



Noise-Induced Tinnitus in Lab Animals

Figure 6. Mice (and rats, not shown) demonstrate acute gap deficits 1-day after noise exposure with background carrier frequencies above trauma frequency (116 dB SPL, 16 kHz octave band for 1 hr). Adapted from Turner et al., in press, J. Neurosci. Research

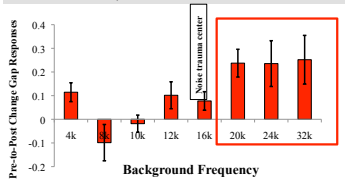


Figure 7. Mice (and rats, not shown) typically recover after the acute tinnitus, until approximately 5-7 weeks later when chronic gap deficits emerge (24 kHz, 60 dB carrier). Adapted from Turner et al., in press, J. Neurosci. Research

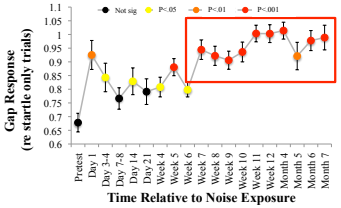
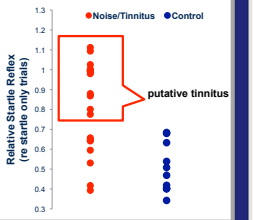
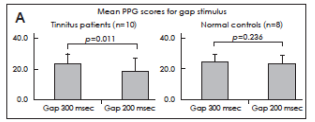


Figure 8. Not every noise-exposed mouse or rat demonstrates gap deficits. Typically, we construct a 95% confidence interval for control responses and define tinnitus as responses worse than the upper limit of that range. This figure represents mouse data but similar effects are observed in rats.



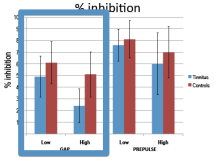
Suh et. al. (2011): Manual Gap Method for Measuring Human Tinnitus

Figure 9. Suh et al. played a 10 dB SL, 8,000 Hz tone to 10 tinnitus participants (all but 1 with tinnitus matched in the 6-8,000 Hz range), and 8 controls. On some trials there was no silent gap, on other trials the gap was 300 ms long, and on some trials the gap was 200 ms long. Participants were to respond manually if they heard the silent gap. Tinnitus participants demonstrated a deficiency in detecting the silent gap in the 200 ms condition. Adapted from Suh et al. (2011) Psychoacoustic characteristics of prepulse gap in tinnitus patients: A preliminary study to develop an objective test detecting tinnitus. Korean J. Otorhinolaryngol-Head Neck Surg 54: 48-54.



Hebert et. al., in progress, Eyeblink Gap Method for Measuring Human Tinnitus

Figure 10. Hebert and colleagues at the University of Montreal measured eyeblink startle response amplitudes in the presence of a low (500 Hz) or high frequency (4,000 Hz) carrier with and without a silent gap embedded in the background, and measured % inhibition of the reflex by the silent gap. The results are still being analyzed (personal communication as of Nov 12, 2011). However, preliminary data shown to the right (presented by Dr. Sylvie Hebert at the 2011 TRI conference in Buffalo and reproduced here with her permission) suggest that participants with high frequency tinnitus might show greater deficits relative to controls in responding to the silent gap when it was embedded in the high frequency carrier that more closely resembled their tinnitus.



Turner, Kinder et. al., in progress, Prototype Gap Method for Human Tinnitus

Figure 11. Turner and Kinder and colleagues have been developing and testing a prototype system for human tinnitus using the eyeblink startle reflex (e.m.g.). Preliminary data have been collected using the same basic methods used in animal studies. A 60 dB SPL background carrier stimulus of 5,000 Hz (1/3 octave) was played into one ear. In half of the trials the startle stimulus was preceded by a silent gap. Tinnitus was then simulated in these normal hearing participants by playing a 10 dB SPL less intense version of the background carrier into the other ear. Preliminary analysis indicates that in participants with otherwise normal silent-gap-induced inhibition of their startle reflex, the addition of simulated tinnitus in the other ear severely disrupted the ability of the silent gap to inhibit the startle reflex.